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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/656,034	09/05/2003	James Hunter Boone	TLAB.100294	8482

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EXAMINER	
VENCI, DAVID J	
ART UNIT	**PAPER NUMBER**
1641	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/656,034	BOONE ET AL.	
	Examiner	Art Unit	
	David J. Venci	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *November 9, 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-14,17-19 and 21-24* is/are pending in the application.

4a) Of the above claim(s) *4,5 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,7-14,17,18 and 21-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-5,7-14,17-19 and 21-24* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges Applicants' reply, filed November 9, 2006, which amended claims 1-3, 11, 12, 17 and 18, and cancelled claim 6 and 20.

Claims 4-5 and 19 remain withdrawn from further consideration pursuant to 37 CFR 1 .142(b) as being drawn to nonelected species.

Currently, claims 1-3, 7-14, 17, 18 and 21-24 are under examination.

Specification

The disclosure is objected to because of the following informalities:

> The information presented in Table 1 does not correspond to information presented in Table 2. Specifically, Table 1 references ~~203~~ 105 patients (*i.e.*, 98 IBD patients (*i.e.*, 47 patients with Crohn's disease + 51 patients with ulcerative colitis) + 7 patients with irritable bowel syndrome) and 11 healthy persons, while Table 2 references 32 patients (*i.e.*, 21 ANCA + UC, 4 ANCA +CD, and 7 IBS) and 11 healthy persons. The disappearance of ~~171~~ 73 patients from Table 2 is not clear.
>
> The information presented in Table 2 does not correspond to information presented in Table 3. Specifically, Table 2 references a total of 43 persons (*i.e.*, 32 patients + 11 healthy persons), while Table 3 references a total of 116 persons (*i.e.*, Total Assessments N = 116). The addition of 73 persons into Table 3 is not clear.

Appropriate correction is required.

Claim Rejections - 35 USC § 112 – second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 11-14 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 3 and 18, the infinitive "to differentiate" is indefinite. Whether the act or process of "differentiating" is completed, performed, or merely intended is not clear. The identity of object(s) and/or step(s), if any, required for performing "differentiating" is not clear.

In claim 11, the preamble phrase "diagnostic assay for determining the optical density of the readable sample" is indefinite. Whether/how "diagnosing" optical density is performed is not clear.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-3, 7-14, 17, 18 and 21-24 are rejected under 35 U.S.C. 101 because the claimed invention lacks credible utility.

Independent claim 1 recites a method for "testing a fecal sample" for anti-neutrophil cytoplasmic antibodies (hereinafter "ANCA"). Independent claim 11 recites a "diagnositic assay for ulcerative colitis". Independent claim 17 recites a method for "screening for ulcerative colitis".

Applicants' specification posits that testing fecal samples for ANCA is specifically useful for "an indicator of ulcerative colitis", "differentiating between ulcerative colitis and Crohn's disease (see Specification, paragraph [0014], first sentence), and "differentially diagnosing ulcerative colitis from... Irritable Bowel Syndrome" (see Specification, paragraph [0009]).

Applicants' assertion of utility is based on data obtained from a clinical study involving patients presenting with "Crohn's Disease" and "ulcerative colitis"[1] and/or "irritable bowel syndrome"[2] (see Specification, paragraph [0017] *et seq.*). In the clinical study, Applicants used standard immunoassay techniques to determine whether fecal samples from patients possessed ANCA.

According to M.P.E.P. 2107.02, Office determination of the credibility of Applicants' assertion of utility is based on whether the facts upon which Applicants' assertion is based are inconsistent with the logic

[1] Crohn's Disease and ulcerative colitis belong to a disease class called Inflammatory Bowel Diseases (IBD). See MeSH Database, Inflammatory Bowel Diseases, *available at* <http://www.ncbi.nlm.gov>.
[2] Applicants' specification does not disclose what standard, if any, Applicants used to identify and include a patient as having "irritable bowel syndrome" into the clinical study.

underlying Applicants' assertion. In other words, credibility refers to the reliability of Applicants' assertion of utility in view of the logic and facts that Applicants offer to support Applicants' assertion of utility.

Here, Applicants' assertion of specific utility is not credible because, according to Table 4 of Applicant's specification, only 41% of patients presenting with ulcerative colitis possessed ANCA (*i.e.*, ANCA is a useful indicator of ulcerative colitis in only 41% of patients). Therefore, based on the data in Table 4, it appears that ANCA is not specifically useful as "an indicator of ulcerative colitis". Necessarily, ANCA is not specifically useful for "differentiating between ulcerative colitis and Crohn's disease or "differentially diagnosing ulcerative colitis from... Irritable Bowel Syndrome".

Claim Rejections - 35 USC § 112 – first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 7-14, 17, 18 and 21-24 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by a credibly-asserted utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Response to Arguments

Specification

In prior Office Action, Examiner objected to the disclosure because:

1. The information presented in Table 1 did not correspond to information presented in Table 3. Specifically, Table 1 references a total of 214 persons (*i.e.*, 203 patients + 11 healthy persons), while Table 3 references a total of 116 persons (*i.e.*, Total Assessments N = 116). The disappearance of 98 persons from Table 3 was considered unclear.

2. In Table 3, the value for Total Assessments N = 116 did not correspond to the number of persons listed in Table 3 (*i.e.*, 98 IBD patients + 47 patients with Crohn's disease + 51 patients with ulcerative colitis + 7 patients with irritable bowel syndrome + 11 healthy persons).

In response, Applicants disclose that IBD patients are "broken down" into CD patient and UC patients (see Applicants' reply, paragraph bridging pp. 7-8, fifth sentence, "the 98 IBD patients were further broken down into 47 CD patients and 51 UC patients").

Insofar as Applicants' disclosure is in accordance with art-recognized disease classifications[3], these objections are withdrawn.

In prior Office Action, Examiner objected to the disclosure because:

1. The information presented in Table 1 does not correspond to information presented in Table 2. Specifically, Table 1 references ~~203~~ 105 patients (*i.e.*, 98 IBD patients (*i.e.*, 47 patients with

Crohn's disease + 51 patients with ulcerative colitis) + 7 patients with irritable bowel syndrome) and 11 healthy persons, while Table 2 references 32 patients (*i.e.*, 21 ANCA + UC, 4 ANCA +CD, and 7 IBS) and 11 healthy persons. The disappearance of ~~171~~ 73 patients from Table 2 is not clear.

2. The information presented in Table 2 does not correspond to information presented in Table 3. Specifically, Table 2 references a total of 43 persons (*i.e.*, 32 patients + 11 healthy persons), while Table 3 references a total of 116 persons (*i.e.*, Total Assessments N = 116). The addition of 73 persons into Table 3 is not clear.

In response, Applicants clarify that Table 2 discloses "all 7 IBS patients tested" (see Applicants' reply, paragraph bridging pp. 7-8, eleventh sentence).

Applicants' clarification is not sufficient to overcome these objections because Table 2 merely discloses a "Number" associated with "IBS", and does not disclose "all 7 IBS patients tested".

Claim Rejections - 35 USC § 101

In prior Office Action, claims 1-3, 6-14, 17, 18 and 20-24 were rejected under 35 U.S.C. 101 because the claimed invention lacks credible utility. Specifically, Applicants' assertion of specific utility is not credible because, according to Table 4 of Applicant's specification, only 41% of patients presenting with ulcerative colitis possessed ANCA (*i.e.*, ANCA is a useful indicator of ulcerative colitis in only 41% of patients). Therefore, based on the data in Table 4, it appears that ANCA is not specifically useful as "an indicator of ulcerative colitis". Necessarily, ANCA is not specifically useful for "differentiating between ulcerative colitis and Crohn's disease or "differentially diagnosing ulcerative colitis from... Irritable Bowel Syndrome".

In response, Applicants argue:

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[3] See *supra*, note 1.

1. despite the mere 41% sensitivity of Applicants' test, Applicants' test is "92% accurate in diagnosing UC (Specificity)" (see Applicants' reply, paragraph bridging pp. 10-11, third sentence).

2. "Only a small fraction of those who test positive for ANCA had another condition or were healthy (8%)") (see Applicants' reply, p. 11, first full paragraph, first sentence).

3. "As such, an elevated level of ANCA can be used to provide a diagnosis of UC in those patients who have an elevated level. As such, when utilized by clinician the method and assay of the present invention, clearly aids a clinician in diagnosing UC rather than diagnosing IBS or CD as very few patients with CD and IBS test positive for ANCA" (see Applicants' reply, p. 11, first full paragraph, second sentence).

Applicants' argument has been carefully considered but is not persuasive.

With respect to 1), Applicants' statement is essentially false because Applicants' test is **not** 92% accurate in diagnosing UC (Inaccuracy). Although Applicants' specification discloses a method having 92% specificity, Examiner posits that, in the instant application, this statistic may be statistically insignificant due to the existence of selection bias (*i.e.*, bias that arises when individuals included in a study are not representative of the target population for the study).[4,5]

With respect to 2), Examiner does not understand the parenthetical "8%", why said parenthetical "8%" is placed in parenthesis, how said parenthetical "8%" departs or digresses from the information presented in the rest of the sentence, or how Applicants derived said "8%" value. Clarification is necessary.

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[4] According to Table 3, the sampled population has a seemingly exaggerated UC prevalence of 82% (*i.e.*, [51 UC patients] divided by [51 UC patients + 11 healthy controls]).

[5] See *also*, Armitage & Colton, *Encyclopedia of Biostatistics*, John Wiley & Sons (1998). According to Armitage & Colton, coverage error (*i.e.*, the difference between statistics based on the population defined by the sampling frame and statistics based on the target population) occurs when there is a lack of correspondence between the frame population and the target population.

With respect to 3), see *supra*, *Claim Rejections - 35 USC § 101*.

Conclusion

No claims are allowed at this time.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Venci whose telephone number is 571-272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

David J Venci
Examiner
Art Unit 1641

djv

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